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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,774	03/13/2003	Tracey Brown	DACO:002US	2305

7590 08/12/2003
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EXAMINER

BERKO, RETFORD O

ART UNIT	PAPER NUMBER
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1615

DATE MAILED: 08/12/2003

6

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/088,774

Applicant(s)

BROWN ET AL.

Examiner

Retford Berko

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13-50 is/are pending in the application.
- 4a) Of the above claim(s) 1-12 are cancelled is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 13-50 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

Acknowledgements

Receipt is acknowledged of the Declaration, Power of Attorney and two Amendments, all filed March 13, 2003.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while arguably enabling for treatment of cancer, does not reasonably provide enablement for the prevention of cancer that includes the prevention of events like tumorigenesis, cell proliferation, metastases, etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C., first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability of the art; (4) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

- (a) The nature of the invention:

The invention provides a method of use of a specific chemical composition, i.e. hyaluronan for sensitizing cancer cells to chemotherapeutic agents during cancer treatment.

- (b) The state of the art:

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The use of chemical compositions for treatment of cancer is known in the art to be effective in certain cancers but prevention of cancer is not yet achieved or demonstrated with any degree of certainty.

(c) The relative skill of those in the art:

The relative skill of those in the art is very high, generally requiring advanced degrees in science and/or medicine.

(d) The predictability or unpredictability of the art:

The Examiner takes the position that it is highly uncertain to predict the onset of cancer and as such the prevention of cancer that necessarily involves the ability to anticipate and counter in advance the onset of the disease is almost impossible to achieve given the present state of the art. However, the Examiner is aware of the remarkable successes in the treatment of specific cancers.

(e) The breadth of the claims:

The claims for prevention of metastases are very broad. A method of inhibiting metastases of cancer cells during chemotherapy with hyaluronan, even if successfully demonstrated is distinguishable from the prevention of cancer and/or the prevention of cell proliferation. The two events are not synonymous and as such a claim for effective inhibition of metastasis that may occur during treatment cannot justifiably support a claim for the prevention of cancer.

(f) The amount of direction or guidance presented:

The specification provides direction for the use of a composition for enhancing anticancer properties of drugs. The specification however provides no direction or guidance on the prevention of metastases or cell proliferation. Because applicant claims the prevention of cancer metastases, the specification lacks direction and guidance in that issues involving the use of the composition for eliminating the onset and/or progression of tumor/host cell interactions, clump formation, antigenicity, adhesiveness and cell surface receptors, organ specificity, relapse rates etc. were not discussed.

(g) The presence or absence of working examples:

The specification describes various embodiments in which in vitro and animal models have been used to demonstrate the enhancement of bioavailability of chemotherapeutic agents when used in combination with the hyaluronan. The specification has enabled one of ordinary skill to use the composition during treatment of cancer but not for prevention of the disease.

(h) The quantity of experimentation necessary:

Given the state of the art in oncology, a person skilled in the art would be burdened with undue "painstaking experimentation study" in order to determine all the necessary events bearing on preventing cancer so as to justify the claims.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13-19, 23-30, 34-35 are rejected under 35 U.S.C. Sec. 102(b) as being anticipated by both Sakurai et. al. [Sho 6191986]-17] and Faulk et al (WO 95/30423, 11/16/1995).

Applicant's claims are drawn to a method of preventing cell proliferation and metastases in mammals including human patients by administration of effective amounts of chemotherapeutic agents and hyaluronan (hyaluronic acid). Sakurai et. al. [Sho 6191986]-17] teach that hyaluronan and its derivatives are effective in drastically reducing metastases of breast cancer cells to the lung in mice. Also, Faulk et.al. teach that administering anti-cancer agents and sodium hyaluronate to a patient with breast cancer was effective in treating the cancer and prevented or reduced metastases in the patient (page 9, lin 5). The disclosures by Sakurai and Faulk render applicants claims anticipated under Sec. 102(b).

3. Claims 36-49 are rejected under Sec. 102(b) as being anticipated by Faulk et. al. (US6,069,135). Applicant's claims are drawn to a method of treating cancer (cell proliferation) in a patient with drug resistant disease by administering effective amounts of a chemotherapeutic agent in combination hyaluronan and preventing metastases of cancer cells to other organs of the body. Faulk et. al. taught that administration of antineoplastic agents in combination with hyaluronic acid was effective in achieving total regression of tumors with lack of metastases to other organs metastasis(col. 21, lin 25).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claim 20-21, 31-33 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harper et. al (US 5, 977,088) in view of Faulk et. al. (US 5, 827,834).

6. Harper et. al. teach that effective amounts of pharmaceutical compositions of hyaluronic acid and /or salts, homologues, analogs, derivatives or esters applied to the skin facilitate the transport of medicines and/or therapeutic agents intradermally into the skin to sites of a pathology and/or trauma to sites of trauma (col. 8, lin 60 and col. 9, lin 60), resulting in successful treatment of the disease or condition at the site of trauma or pathology including basal cell carcinoma, metastatic cancer of the breast to the skin and metastatic melanoma. Harper neither specifically teach the use of pharmaceutical compositions with hyaluronic acid as an excipient for elimination of the onset of metastases of cancer cells to other organs nor does it teach the use of hyaluronic acid immediately before or after the drug administration to overcome drug resistance.

7. Faulk et. al. teach that administration of a combination of antineoplastic agent mixed with hyaluronic acid to a patient who had advanced carcinoma of the bladder with metastases to the pelvis leads to regression of previously unresponsive tumors when hyperthermia was applied to the pelvis area. Faulk also taught the use of hyaluronic acid either before or after the administration of the antineoplastic agent. While Faulk alludes to the fact that hyaluronic acid

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may improve the penetration of the drug through the skin, Faulk does not specifically teach that hyaluronic acid improves bioavailability of antineoplastic agents to improve or prevent metastases when it is applied to the skin.

8. In order to obtain inhibition of cell proliferation during treatment of cancer, one of ordinary skill in the art would have expected to use hyaluronan in combination with cancer drugs to treat a patient with cancer of the breast, lung, prostate, kidney, ovary or other forms of cancers as claimed by applicant because both Sakurai and Faulk showed that the combination is efficacious. The use of a combination of antineoplastic agents with hyaluronic acid would be expected to produce successful regression of the tumors because of improved bioavailability of the drug effected by hyaluronic acid. Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made by the applicant only as far as it pertains to treatment and not prevention of cancer.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Retford Berko whose telephone number is 703-305-4442. The examiner can normally be reached on M- F 8:00 a.m.- 5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-9903 for regular communications and 703-746-9903 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600